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## Review Article

# Dairy-Derived Nutrients and Cognitive Aging: Evidence from Observational and Experimental Studies

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### ABSTRACT

The growing burden of cognitive impairment and Alzheimer's disease calls for the development of simple, dietary approaches to protect against cognitive decline. Dairy foods are a complex nutritional matrix, containing lipids, micronutrients and fermentation products which may interact to influence brain ageing via multiple mechanisms. Here, we critically evaluate the existing evidence on dairy consumption and cognitive performance, focusing on dose-response, food matrix effects and emerging neurobiological mechanisms. A systematic review of epidemiological and experimental research shows a clear nonlinear (inverse U-shaped) relationship between total dairy intake and cognitive function. Modest intakes (1-2 servings per day) are linked with optimal cognitive function and protection against cognitive impairment, especially in populations with low dairy intakes, while high intakes provide no further benefit, and may be harmful. The strongest and most consistent cognitive effects are observed with fermented dairy products (yogurt, cheese), likely due to interactions between probiotics, bioactive peptides, and lipid remodeling that affect the gut-brain axis, neuroinflammation and synaptic plasticity. By contrast, results for milk are mixed and sweet dairy products diminish benefits. Functional studies demonstrate the cognitive-enhancing effects of dairy peptides like  $\beta$ -lactolin that regulate monoamine activity and enhance memory-related brain activity, especially in early cognitive impairment. However, few randomized controlled trials with dairy foods limit causal inferences. Areas of future research include controlled dietary interventions combined with neurocognitive, metabolomic and microbiome analyses. In conclusion, regular moderate intake of fermented dairy products may have beneficial effects on cognitive function and slow neurodegenerative processes and improve quality of life in the elderly.

## INTRODUCTION

As the world's population ages, cognitive impairment and dementia, especially Alzheimer's

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disease (AD), place an increasing burden on individuals, families and health care. AD, a neurodegenerative disease that affects more than 55 million people globally (and is expected to triple by 2050), is characterised by memory loss, confusion, poor judgement and language impairment. (1)(2)

The disease is characterised by amyloid- $\beta$  (A $\beta$ ) plaque formation, hyperphosphorylated tau protein, mitochondrial dysfunction, and persistent neuroinflammation, mediated by activated microglia, which secrete pro-inflammatory cytokines (e.g., TNF- $\alpha$ , MIP-1 $\alpha$ ), reactive oxygen species (ROS) and nitric oxide (NO), leading to neuronal cell death. In the absence of effective disease-modifying treatments, primary prevention, focusing on modifiable risk factors like diet, has emerged. Epidemiological studies associate dairy products (e.g., low-fat yogurt and cheese) with lower cognitive decline and AD risk; for example, weekly dairy intake is associated with better cognitive performance, improved memory, social interaction and reduced stress.(4, 1,2)

Neuroprotective dairy bioactives (e.g., calcium, B vitamins, milk fat globule membrane (MFGM), phospholipids, fermented peptides) have antioxidative, anti-inflammatory properties, and influence the gut-brain axis. This is consistent with cognitively protective dietary patterns (e.g., Mediterranean, DASH, MIND diets) that include moderate dairy consumption (1-2 servings/day) and fruits, vegetables, and grains. (3,5)

Most research is conducted in low-dairy Asian populations (6)(e.g., Japan, South Korea(7,8), Taiwan (9), Singapore (10), China (13,14), but it's difficult to tease apart dairy's specific role.

This review examines epidemiological, clinical and mechanistic studies on dairy intake across the lifespan and its impact on late-life cognition. A systematic search of Web of Science, PubMed, PsychINFO, and Scopus databases with keywords "(dairy OR milk OR cheese OR yogurt) AND ('mild cognitive impairment' OR dementia OR 'Alzheimer's disease')" identified 796 articles after removing duplicates; 574 articles were excluded following title/abstract screening for irrelevance (e.g., non-elderly, unrelated diseases such as Parkinson's, or non-dairy interventions).(55)

The remaining articles feed into dairy's incorporation into overarching models, with a focus on bioactives, fermentation, gut-brain axis, and population-specific factors to inform nutritional strategies for brain ageing and AD prevention.(55)

The abstracts of the remaining 222 articles were examined and classified as research summaries (literature reviews and meta-analyses) and original research. Original research was further divided into preclinical (in vitro and animal) studies and human studies. A further 37 articles were excluded as irrelevant (e.g., chemical composition of dairy products not related to cognition). The 51 remaining human studies were critically assessed and categorised as observational studies on the association of dairy intake with cognitive function in the elderly, or intervention (experimental) studies on the effects of dairy on cognitive function. Additional exclusions (n=22) included studies on combined dietary patterns that obscured the effects of dairy or those that used unvalidated measures of cognition (e.g., neuroimaging only). Finally, 23 observational and 6 intervention studies were synthesised in the following Sections.(55)



## Observational Studies

Many observational studies have examined the link between dairy intake and cognitive function in older adults. The 23 studies identified used three main designs, with varying levels of rigour.

The weakest are cross-sectional studies, which examine dietary intake and cognition at the same time, preventing the determination of a temporal link and causality. Reverse causality is possible, with cognitive decline potentially affecting dietary recall.

Retrospective cohort studies are better, as they examine dietary data from the past and cognitive data from the same time period, but are constrained by data integrity, as records were not collected for research.

Prospective cohort studies are considered ideal, as they assess dairy intake at baseline and cognitive function over time, allowing temporal inference.

The majority of studies have grouped dairy products into a single category. But some studies focused on milk, high-fat dairy or fermented dairy. Results are summarised by category in subsections below; studies encompassing multiple categories are included in relevant section.

The available evidence on total dairy-product intake and cognitive function shows a nonlinear (inverse U-shaped) relationship, with moderate intake associated with best outcomes.

### Total Dairy Product

The available evidence on total dairy-product intake and cognitive function shows a nonlinear (inverse U-shaped) relationship, with moderate intake associated with best outcomes.

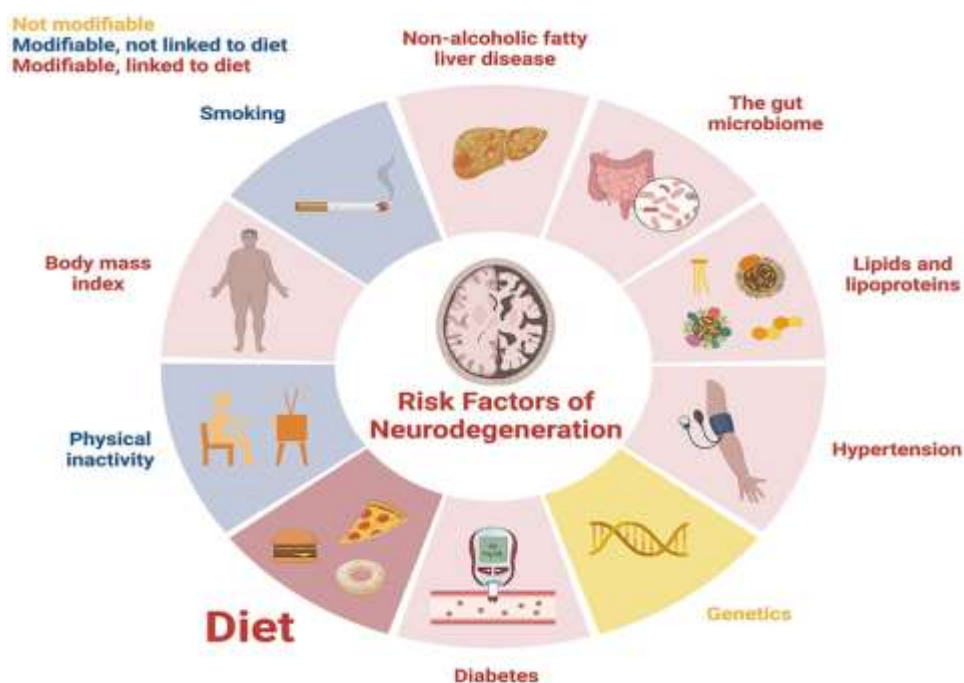


FIGURE.2

Risk factors for the development of neurodegeneration in later life. Image adapted from a template using BioRender.com

### Cross Sectional Studies

Of the 10 cross-sectional studies that examined the association between participants' current diet and cognition, six found a positive association between dairy intake and cognition, two found no association, and two found a negative association. Two positive studies were in South Korea. In the first, the prevalence of low cognition ( $MMSE \leq 19$ ) was greater in women than men (31% vs. 22%) (15). Women with low cognition ( $MMSE \leq 24$ ) had lower dairy consumption than women with normal cognition (Cohen's  $d = 0.56$ ); this was not found in men. In the second study, sufficient dairy intake decreased MCI risk ( $MMSE = 20-23$ ) by 90% [adjusted odds ratio (AOR) = 0.100] (20).

Other Asian studies had positive results. A Taiwanese study showed higher daily dairy intake scores (1/day) in those with normal vs. impaired

cognition (43% vs. 37%) (16). A Chinese study found higher dairy intake reduced the odds of MCI by 35% (25), but had different effects on different MCI subtypes: amnesic MCI (OR = 1.51) and non-amnesic MCI (OR = 0.49). Two other studies showed smaller positive effects. One US study found dairy intake associated with better episodic memory (Cohen's  $d = 0.16$ ) (16). A Canadian study showed total dairy intake correlated with executive function (partial  $\eta^2 = 0.001$ ) (26).

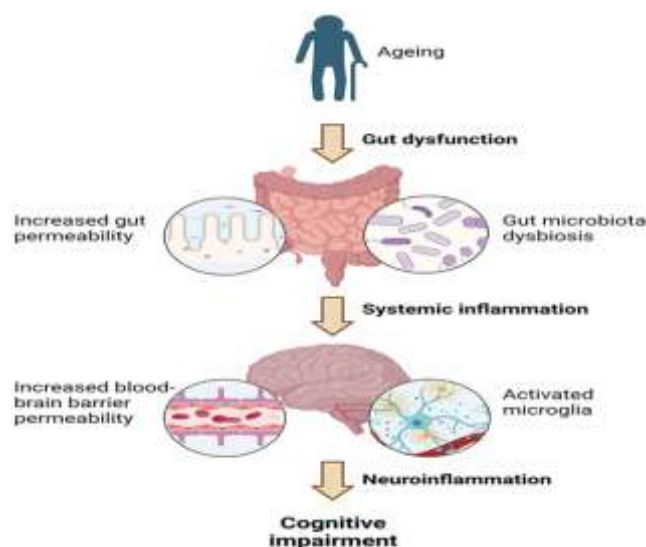
Two studies showed no correlation. A crude Central African study found no difference in dementia incidence between daily and non-daily dairy consumers (19), perhaps due to dichotomous analyses. A sophisticated Dutch study also detected no associations in various cognitive domains (21).

Finally, two studies found negative links. A US study found high dairy intake (Q4) was associated with lower composite cognitive scores vs. low intake (Q1) after adjusting for confounders ( $\beta = -0.13$ ) (23), with medium ( $\beta = -0.27$ ) and large ( $\beta = -0.6$ ) effects on recall and delayed recall,

respectively. A Spanish study found high intake (Q4) linked to a 40% increased risk of cognitive decline (25).

Differences are probably due to different dairy intakes. Studies with positive effects (particularly Asian) had lower intakes: 35 g/day (13); 0.9 times/day (20); 77 g/day (24) [intake not reported by Chen et al. (15)]. Small positive effects occurred at higher levels: median 78 g/day (Q4 > 163 g/day) (16); median 1.9 times/day (Q4 > 2.5 times/day) (26). Negative-effect studies had much higher intakes: Q4 > 12.8 g protein/day (376 mL milk/day) vs. Q1 < 4 g (117 mL) (22); Q4 ≥ 500 g/day vs. Q1 < 200 g/day (25).

These findings are consistent with an inverse U-shaped curve, with moderate dairy intakes (1-2 servings/day) being optimal for cognitive function



**FIGURE.3. The proposed pathway by which age-associated gut dysfunction may contribute to cognitive impairment. Image created using BioRender.com.**

Study Type	Typical Intake (Positive/Optimal)	Typical Intake (Negative/High)
Asian	35–77 g/day or ~1 serving/day	N/A
Western	Median 78 g/day; Q4 >163 g/day	>376 ml milk/day or ≥500 g/day

## Prospective cohort studies

The remaining published observational studies that have investigated the association between dairy product consumption and cognitive function in older age were prospective cohort studies. Three of these found higher dairy intake was associated with lower risk of cognitive impairment or dementia.

## Dairy intake and reduced cognitive impairment

In a Japanese study, women with high dairy intake had 23% lower odds of cognitive impairment over 10 years than women with low dairy intake (odds ratio ≈ 0.77) (17); this effect was not seen in men. Dairy intake was dose dependent in another Japanese study over 18 years (18). Compared with the lowest quartile of dairy intake (Q1: <45 g/day for women and <20 g/day for men), the middle quartile (Q3: 97-197 g/day for women and 76-173 g/day for men) had a lower overall risk of dementia [adjusted hazard ratio (HR) ≈ 0.66], while the Q2 and Q4 quartiles did not differ from Q1, suggesting an inverse U shaped association between dairy intake and dementia risk.

## Evidence from Singapore and Western populations

This study was further supported by a recent larger prospective cohort study in Singapore (23). The median dairy intakes in this cohort were relatively low (Q1-Q4: 5.68, 9.41, 36.6 and 252 g/day). During the 20 year follow up, the Q3 and Q4 dairy intake groups had 16% and 21% reduced odds of cognitive impairment compared to the lowest intake group, respectively. However, a Finnish prospective cohort study found no association between total dairy intake and either the risk of dementia or cognitive tests (27). The dairy intake in this Finnish cohort was much higher than that in the Asian studies (Q1 <455 g/day and Q4 >927

g/day; median intake in Q1 was 292 g/day, compared to the median intake in Q4 in the Singapore study by Talaei et al. (23)

### Interpretation of heterogeneity across studies

The association between dairy consumption and later life cognition seems to be dependent on the range of dairy intake in the study population, with protective effects mainly seen at lower levels of

dairy intake, and no or even inverse associations at higher levels. Moreover, differences between studies may also be due to variations in dairy subtypes (e.g., full fat milk, fermented dairy, low fat dairy) consumed, as recent evidence indicates that different dairy subtypes may have different effects on cognition. Thus, the next subsections discuss the association between different dairy subtypes and cognition.(12)

Population / study	Intake range (g/day)	Cognitive outcome vs. lowest quartile	Key effect size
Japanese women	Higher (Q) vs. lower	23% lower odds of 10-year cognitive decline	OR $\approx$ 0.77 [par]
Japanese (Q3)	76–197 (men/women)	34% lower dementia risk over 17 years	HR $\approx$ 0.66 [par]
Singapore (Q3–Q4)	Up to 252 g/day	16–21% lower odds of cognitive impairment over 20 years	OR $\approx$ 0.79–0.84 [par]
Finnish (Q1–Q4)	292–>927 g/day	No association with dementia risk or cognitive test performance	NS [par]

### Milk

There have been ten observational studies of the association between milk consumption and cognitive function, which do not specify milk type, but are likely to be cow's milk. Bovine milk is typically made up of 4.6% lactose, 3.4% protein, 4.2% fat, 0.8% minerals and 0.1% vitamins. The design of these studies is outlined in five were cross-sectional, one was retrospective cohort and four were prospective cohort. This mix of study designs permits assessment of cross-sectional (concurrent) and longitudinal (retrospective and prospective cohort) associations between milk and cognition.

### Cross sectional studies

Four cross sectional studies found no significant association between milk intake and cognition. Park and Fulgoni (16) found no difference in the scores for the cognitive tests between people who reported no, low, moderate, or high milk intakes.

Similarly, Rahman et al. (30), Tessier et al. (26), and de Goeij et al. (21) did not observe any change in the odds of low cognitive test scores with milk intake. However, in two of these studies, total dairy intakes were positively associated with cognitive test scores (16, 26), so the benefits may have been due to dairy products other than milk.

However, one cross sectional study reported an association between milk intake and cognition. Kim and Yun (20) found that the odds of mild cognitive impairment (MCI) decreased by 58% when milk intake increased to once per day (adjusted odds ratio  $\approx$  0.42). The mean milk intake in this study was low (0.36 servings/day), while in the Tessier et al. (26) study the mean milk intake was much higher (0.89 servings/day). The four cross sectional studies that did not find a relationship between milk intake and cognition did not report ranges of daily milk intakes (16, 21, 30), but total dairy intakes in the Western based cohorts were higher than in the South Korean study by Kim and Yun (20). Taken together, these results

indicate that increasing milk intake from low to adequate intakes may be beneficial for cognition, but higher intakes do not seem to have further benefits.

Aspect / study	Intake type	Cognition finding	Notes
Park and Fulgoni	Milk intake	No association with cognitive test scores	No differences across none/low/moderate/high milk consumption levels.
Rahman et al.	Milk intake	No association with risk of low cognitive scores	Null finding for milk, but total dairy intake was positively linked to cognition.
Tessier et al.	Milk intake	No association with risk of low cognitive scores	Mean milk intake = 0.89 servings/day; total dairy associated with higher scores.
de Goeij et al.	Milk intake	No association with risk of low cognitive scores	Daily milk-intake ranges not reported; total dairy linked to better cognition.
Park and Fulgoni , Tessier et al.	Total dairy intake	Positive association with cognitive test scores	Suggests benefits come from non-milk dairy products (e.g., yogurt, cheese).
Kim and Yun (South Korea)	Milk frequency	58% lower risk of MCI at about 1 serving/day	Baseline milk intake low (0.36 servings/day); benefit seen when increasing from low to once-daily intake.
Western vs. Korean studies	Total dairy intake	Higher in Western studies than in the South Korean study	Supports a threshold-like effect: going from low to adequate milk/dairy may help, but higher than adequate intake adds no extra benefit.

### Prospective cohort studies

Milk intake during mid life and cognitive performance in later life was evaluated in four prospective cohort studies with varying results.

### Inconsistent milk intake-dementia associations

A Japanese study found that mid life milk intake almost every day was associated with a 74% reduction in the risk of vascular dementia in later life compared with those who drank milk less than twice a week (adjusted hazard ratio  $\approx 0.26$ ) (28). But there was no association between milk intake and Alzheimer's disease (AD). However, three other prospective studies reported higher mid life milk consumption was associated with poorer cognitive function. In a study of Australian men, regular milk drinkers had a 31% greater risk of cognitive impairment (Mini Mental State Examination (MMSE)  $< 24$ ) five years later than non regular milk drinkers (29). In another US study, daily milk consumers had a 11% faster

decline in cognitive function over 20 years than non regular milk drinkers (32). The Finnish cohort by Ylilauri et al. (29) observed no association between milk consumption and risk of dementia or AD, but did observe 8.6% lower average verbal fluency scores in the high milk intake group compared with the low intake group.

### Potential explanations for heterogeneity

Heterogeneity in milk intake levels can not explain the differences between studies, as two studies with negative associations (29, 32) compared regular/daily milk intake with rare or no milk intake, the same comparison used in the study by Yamada et al. (28) that found a protective effect. The differences in the cognitive measures and definitions of cognitive impairment probably play a role. While Ylilauri et al. (27) and Yamada et al. (28) mainly studied clinically diagnosed dementia, Almeida et al. (29) included participants with mild cognitive impairment (MMSE  $< 24$ ) and Petruski Ivleva et al. (32) studied longitudinal changes in

cognition, it is possible that milk may protect against vascular dementia or AD but not against MCI; this needs to be further explored.

### Role of gender and study population

The role of gender may also play a role. The Finnish (27) and Australian (29) studies were

conducted in men only, the US study (32) did not report sex stratified analyses, and 67% of the Japanese study (28) participants were women. This suggests that increased milk consumption may be more protective for women than men, but more sex stratified analyses and studies in different populations are required to confirm this.

Study	Country	Population	Milk Intake Comparison	Key Cognitive Outcome	Result
Yamada et al.	Japan	Mixed (67% women)	Daily vs. <2x/week	Vascular dementia risk	74% lower risk (protective)
Almeida et al.	Australia	Men only	Regular vs. rare/none	Cognitive impairment (MMSE <24) at 5 years	31% higher risk
Petruski-Ivleva et al.	USA	Gender NR	Daily vs. rare/none	Cognitive decline over 20 years	11% greater decline
Ylilauri et al.	Finland	Men only	High vs. low	Verbal fluency scores	8.6% lower scores (no dementia/AD link)

### Dairy lipids

A potential explanation for the variability in the findings between observational studies in different populations is the proportion of full fat versus skim (low fat) dairy consumed. Lipids make up around 50% of the dry weight of the human brain and dietary lipids derived from dairy products are known to be essential for normal brain development in early life (33). Therefore, it is possible that dairy derived lipids may also play a role in maintaining cognitive function in later life.

A review of the literature found seven observational studies that specifically investigated dairy lipids and cognition in older age. These studies are outlined and are described below in sub-sections based on whether they compared full fat versus skim dairy consumption, high fat dairy desserts, or specific dairy lipid compositions (e.g., saturated fat, phospholipids or fatty acid profiles) with cognitive function.(34)

### Full-fat dairy

Four cross sectional studies explored the associations between full fat and skim dairy products and cognition separately, with conflicting results. In the study by Muñoz Garach et al. (25), total dairy intake was positively associated with the risk of mild cognitive impairment (MCI). But moderate consumption of full fat milk and dairy products was associated with a reduced risk of cognitive impairment (27% for quintile Q2 and 26% for Q3 relative to Q1), suggesting that dairy lipids may play a role in the protective associations.

However, the results from two other studies suggest that dairy intake may have a positive effect on cognitive function via mechanisms unrelated to lipids. In the study by de Goeij et al. (21), which found no associations between total dairy intake or milk intake and overall cognitive scores, a small positive association was reported between skim dairy intake and executive function ( $\beta = 0.07$ ), but no association between full fat dairy intake and cognitive function. Similarly, Tessier et al. (27) found that higher low fat dairy intake was associated with slightly higher executive function

scores (partial  $\eta^2 = 0.002$ ), but there were no differences between full fat dairy intake groups.

The findings of these three studies may have been affected by the inclusion of fermented dairy products, which vary in their nutrient and bioactive content. In a comparison of total milk, semi skim/skim milk and full fat milk, with the only difference being the fat content, de Goeij et al. (21) reported no associations with any cognitive domain scores. In line with this, a Brazilian study (37) found no differences in cognitive function between skim and full fat milk consumers. These results indicate that the cognitive effects of dairy intake may be related to overall dairy intake and possibly other dairy components (e.g. proteins or compounds related to fermentation) rather than the fat content.

### High-Fat Dairy Desserts

In a French prospective cohort study of women, dairy desserts were examined separately from other dairy products because of confounding. Women in the 60s with above-median dairy dessert and ice cream consumption had a 33% increased risk for cognitive impairment in late life compared with non-consumers (HR = 1.33; (36). The link with pastries/cakes was close to significant ( $P=0.056$ ). Since dairy desserts/ice cream and pastries/cakes are rich in refined sugars, the risks are unlikely to be due to dairy fat. This is consistent with Tessier et al. (26), who excluded dairy desserts from the total dairy analyses because of high refined sugar content.

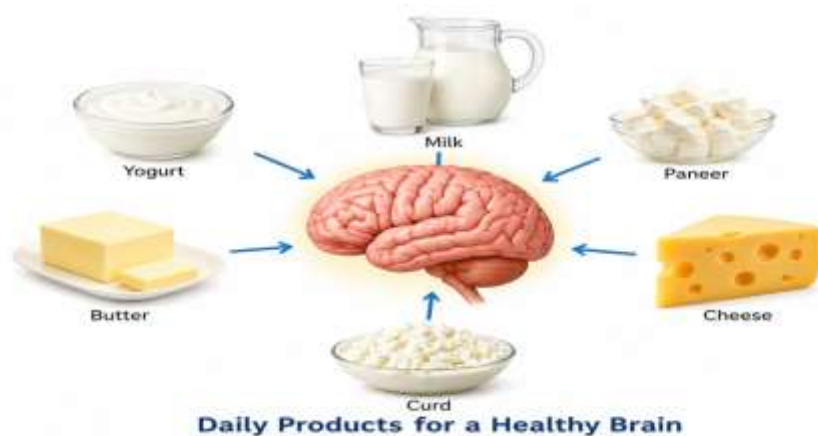
Study	Population	Exposure	Outcome	Result	Confounder Note
French study	Women only	High-fat dairy desserts/ice cream (>median vs. none)	Cognitive impairment	33% higher risk	Refined sugars
French study	Women only	Pastries/cakes	Cognitive impairment	Near-significant ( $P = 0.056$ )	Refined sugars
Tessier et al.	[NR]	Desserts excluded from total dairy	Executive function	[Supports exclusion]	Refined sugars

### Fermented Dairy Products

Fermented dairy products are fermented milk products. Examples are yogurt and cheese, but also buttermilk, sour cream and crème fraiche. The fermentation is usually due to lactic acid bacteria (LAB). Many LAB strains are good for health. So, health benefits may be caused by the dairy

product, the live bacteria or the dead bacteria (or parts of the bacteria such as surface molecules).

Studies on Cognitive Function in Older Adults , There are seven studies on fermented dairy products and cognitive function in older adults. We've grouped them by product below.



**FIGURE 3.**Freepik, 2024. Dairy products and brain health concept. [online image] Available at: <https://www.freepik.com/> [Accessed 28 April 2026].

### Total fermented dairy

Three cross-sectional studies have investigated fermented dairy products as a group, with conflicting findings. Two studies found small positive associations with executive function: de Goeij et al. (21) reported a small positive association with higher fermented dairy intake ( $\beta=0.06$ ), which was similar to skim dairy but not total dairy; similarly, Tessier et al. (26) reported higher intake was associated with better executive function scores (partial  $\eta^2=0.002$ ). However, Muñoz-Garach et al. (25) found high fermented dairy intake (Q4) was associated with a 34% higher risk of low MMSE scores ( $\leq 26$ ). These conflicting results probably reflect the cognitive tests used; the first two studies focused on executive function, while the latter used the MMSE, which does not include executive tasks. A prospective study (26) also reported no link between midlife fermented dairy intake and later-life dementia risk or cognitive function (including executive function), suggesting no long-term benefits. Further studies are needed to clarify these findings.

### Cheese

Cheese is a fermented milk product containing high levels of saturated fatty acids (SFA; ~15% -

25% of total fat depending on the cheese variety) that has been linked to cognitive impairment, as noted above. However, the six studies of cheese intake and cognitive performance in older adults all found positive associations. Four were cross-sectional and cannot be used to infer causality.

One U.S. study that separated cheese intake from milk intake found that increased frequency of cheese intake was associated with 32% lower odds of cognitive impairment (34,35), but milk intake was not. Similarly, Park and Fulgoni found slightly better episodic memory in cheese consumers compared to non-consumers (Cohen's  $d = 0.12$ ); total dairy intake had similar effects, but milk intake showed no association. de Goeij et al.(21) found no association between total dairy intake and cognitive domains, or total cheese intake and processing speed, but Dutch cheese intake was associated with 33% reduced odds of low processing speed; skim milk intake was associated with better executive function (30). Tessier et al. reported higher dairy intake associated with better executive function, but not milk, and cheese intake associated with slightly higher executive function scores (partial  $\eta^2 = 0.001$ ,  $P < 0.001$ ).

Variations in affected cognitive domains could be due to different cognitive tests used. Two

prospective cohort studies supported these findings: a U.K(16). study found higher cheese intake linked to higher Fluid Intelligence Test scores ( $\beta = 0.207$ )(38), which measure executive function and problem-solving ; a Finnish study found no total dairy-dementia association and lower verbal fluency with milk intake, but moderate cheese intake (Q3) linked to 17% lower dementia risk compared to low intake (Q1) (27).

## Yogurt

Yogurt, a fermented milk product containing lower saturated fatty acids (SFA) than cheese, may contain probiotic bacteria that have been selected for health-promoting properties - especially in Asia. But sugars in some products may have a negative impact on cognition.

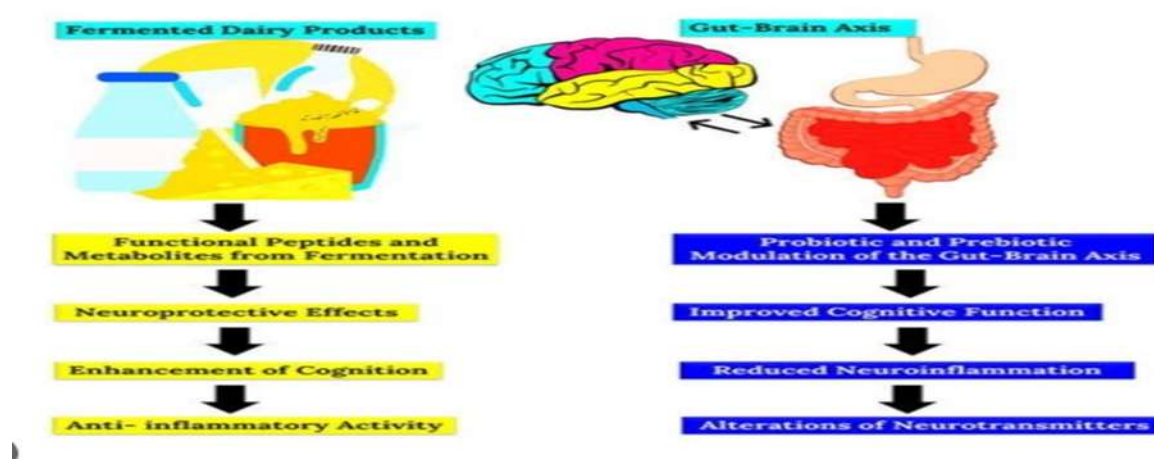
Three cross-sectional studies had mixed findings on yogurt and late-life cognition. Kim and Yun (20) found yogurt was associated with 74% reduced odds of mild cognitive impairment (MCI). Tessier et al (26). reported yogurt associated with slightly improved memory (partial  $\eta^2 = 0.001$ ), but not cheese which was associated with improved

executive function. On the other hand, de Goeij et al (21). found no associations between total yogurt consumption and performance in cognitive domains (all  $\beta P > 0.05$ ).

These differences may reflect yogurt differences (sugar, probiotics) or consumption patterns. For example, in South Korea where greater benefits were observed, probiotic-rich liquid yogurt drinks are more popular than in the West.

## Buttermilk

Buttermilk is a fermented dairy product that is low in SFA and sugar and thus may be more advantageous than cheese and yogurt. But buttermilk was only considered in one study. As mentioned above, de Goeij et al (22). reported minor improvements in executive function with fermented dairy ( $\beta = 0.06$ ), which were not explained by yogurt or cheese (both  $\beta P > 0.05$ ). Buttermilk consumption was specifically associated with greater improvements ( $\beta = 0.10$ ), and may be the driver of these effects. These results need to be replicated.



**Figure 4.** Conceptual illustration of how fermented dairy products contribute to cognitive health through two major mechanisms: (1) the generation of neuroactive peptides and anti-inflammatory metabolites during fermentation, and (2) probiotic and prebiotic modulation of the gut-brain axis, enhancing cognition, reducing neuroinflammation, and influencing neurotransmitter dynamics. image created with

www.biorender.com

## Experimental studies

There are only a few experimental studies that have examined the impact of dairy-derived products on cognitive function in the context of aging, and to our knowledge, no published trial has used a dairy product (milk, yogurt, or cheese) as the main dietary intervention to study cognitive aging. Rather, all existing experimental studies have investigated the effects of dairy-derived bioactive peptides, especially those produced by fermentation or enzymatic digestion of milk proteins, which are delivered as purified or enriched preparations, rather than whole foods.

### $\beta$ – lactolin

Three experimental studies have used a dietary intervention of a whey peptide mixture, derived from the enzymatic digestion of whey protein, in which the proposed active ingredient  $\beta$ -lactolin (Gly-Thr-Trp-Tyr) comprises 0.16% of the mixture (40,41,42).  $\beta$ -Lactolin is a tetrapeptide naturally produced during the fermentation of whey by the yeast *Penicillium candidum* (as occurs in Camembert and blue cheeses) and has been proposed to enhance cognitive function by modulating central monoaminergic pathways.

Each of the three randomized, placebo-controlled studies reported greater enhancements in specific cognitive domains following the whey peptide intervention containing  $\beta$ -lactolin than following placebo. The first two studies involved adults aged 45-65 years with self-reported memory complaints(40); although no between-group differences in global cognitive function were reported, a prespecified subgroup analysis found that participants with high baseline fatigue showed greater improvements in executive function after six weeks of  $\beta$ -lactolin supplementation compared with placebo (verbal fluency "a" score, Cohen's  $d = 0.73$ ; Stroop test step 3 errors, Cohen's  $d = 0.67$ ).

This effect was confirmed in the second study, which found that six weeks of  $\beta$ -lactolin significantly increased verbal fluency "a" scores from baseline (Cohen's  $d = 0.83$  for the change score(44), but not in the placebo group.

The third study examined older adults (50-75 years) and found domain-specific improvements in cognitive performance following six weeks of  $\beta$ -lactolin supplementation compared with placebo(42). In particular,  $\beta$ -lactolin enhanced performance on the visual paired-associates I task (Cohen's  $d = 0.45$ ), which assesses visual associative memory and new learning, and decreased time to complete the visual cancellation task (Cohen's  $d = 0.44$ ), which assesses selective visual attention. These cognitive enhancements were accompanied by neurophysiological evidence of greater activation in the parietal region during auditory attention and sustained attention tasks, suggesting a possible mechanism for the cognitive improvements

### Proline-Rich Peptides

Three intervention studies have used dairy-derived proline-rich peptides as the active agent. One study examined colostrinin, a mixture of proline-rich polypeptides derived from ovine colostrum, while the other two studies examined lactotriptides (Val-Pro-Pro and Ile-Pro-Pro) produced by fermentation of casein by lactic acid bacteria, and the casein-derived tripeptide, Met-Lys-Pro (MKP).

In the first study, patients aged  $\geq 50$  years with probable Alzheimer's disease (AD) were supplemented with colostrinin(39) for 15 weeks. Colostrinin stabilized a number of global cognitive measures that worsened in the placebo group, with subgroup analyses suggesting greater benefits in subjects with mild cognitive impairment than in those with moderate or severe impairment,



suggesting greater efficacy of early intervention. But effect sizes could not be calculated due to missing standard deviations (41,42).

The other two studies showed no significant cognitive effects. Hamasaki et al. (41) examined the effects of lactotriptides on brain oxygenation in healthy adults >50 years, with Stroop test performance as a secondary measure. Lactotriptides enhanced prefrontal cortex oxygenation at rest and during exercise compared to placebo, but there were no differences in Stroop test performance. Yuda et al. (43) investigated the MKP peptide in healthy adults >40 years, and found no overall cognitive differences compared to placebo; age-stratified analysis (>65 years) showed no improvement in global measures and only small improvements in two subtests (Constructions, Cohen's  $d = 0.29$ ; Orientation, Cohen's  $d = 0.34$ ). The absence of strong effects in these studies may reflect ceiling effects in cognitively intact adults, in whom it is challenging to detect subtle changes. Longitudinal studies examining the effects of proline-rich peptides during mid-life are therefore needed to determine whether these supplements can prevent cognitive decline in later life.

## CONCLUSIONS AND FUTURE DIRECTIONS

### Summary of Evidence

This review provides an overview of observational and experimental studies showing moderate dairy intake (about one serving per day) has a beneficial effect on cognitive function in older age. This effect is greatest in Asian populations with low dairy intakes where increases to moderate intakes are beneficial (e.g., cross-sectional studies). In Western populations with higher baseline intake, high intakes (>2 servings per day) have a lesser or

null effect, indicating an inverse U-shaped dose-response curve.(14,17,18,20,23,24)

Milk results are mixed: cross-sectional studies support benefits in low-intake Asian populations, but three of four prospective studies report higher mid-life milk intake is associated with increased risk of cognitive impairment in later life. A retrospective study shows benefits from childhood milk. Thus, milk is unlikely to be the main source of moderate total dairy benefits(22,25-27)

Dairy lipids have mixed effects, possibly due to fermented dairy. Low- versus full-fat milk has no cognitive effect, and dairy desserts with high-fat increase risk, likely due to sugars. One study suggests dairy polyunsaturated (PUFA) and monounsaturated (MUFA) fatty acids (FA) protect against Alzheimer's disease (AD) and mild cognitive impairment (MCI), while saturated (SFA) are risk factors.(34,35)

Fermented dairy (cheese, yogurt, buttermilk) has the most consistent, positive associations. Of three studies examining total fermented dairy, two show improved executive function, while one shows decreased function(21,26). Cheese shows consistent positive associations in six study, with Dutch cheese being particularly positive, perhaps due to high vitamin K2 levels . Yogurt is mixed (positive in two studies ; neutral in one ), perhaps due to varying sugar levels. Buttermilk enhances executive function in one study (21). Confounder adjustment (e.g., age, sex, education, BMI, socioeconomic status (Townsend Index , poverty-income ratio , or income) shows cheese benefits are not confounded.

### Limitations of Observational Data

Diverse outcomes (e.g., dementia/AD vs. MCI; MMSE vs. domain-specific tests) and study designs (prospective vs. cross-sectional) make



comparisons difficult. Longitudinal studies suggest a preventive effect, but cross-sectional studies can't separate lifelong protective vs. acute therapeutic effects. Longitudinal studies will resolve lifelong diet effects.(46,38)

### Evidence from Interventions

Six intervention studies using dairy peptides (fermentation products) show improved cognitive function in impaired adults (four studies) but not in healthy adults (two studies), suggesting they may be early interventions. (49,51,54,35)

### Future Research Directions

Randomized, double-blind, placebo-controlled studies with dairy products are needed. Prophylactic effects could be studied with long-term (>10 years) trials of low/moderate/high intake, but are difficult to conduct. Brief interventions in cognitively impaired adults with low intake are more practical to assess therapeutic effects, favouring fermented dairy products.(38)

Mechanistic studies should combine dietary/cognitive measures with microbiota profiling, gut permeability and inflammation markers, as there is evidence for microbiota changes and neuroinflammation reduction. Dairy lipids are modified by bacterial metabolism (e.g., 2-fold higher triglycerides in yogurt, 10-fold in cheese compared to milk), so lipidomics should be considered.(21,24,26)

This narrative review offers a broad overview of study designs but not meta-analysis. Bias was reduced with a pre-specified search strategy.

Overall, moderate intake (1-2 servings/day) of fermented dairy products, particularly cheese, lowers risk of cognitive impairment in later life. Whole product interventions should be

experimentally validated to guide dietary recommendations for healthy brain aging.

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